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Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

SUBJECT: DOCKET NO. 00D-1407
INTERNATIONAL CONFERENCE ON HARMONISATION:DRAFT GUIDANCE ON SAFETY PHARMACOLOGY STUDIES FOR HUMAN PHARMACEUTICALS

Dear Sir or Madam:

On August 7, 2000, FDA announced the availability of the draft guidance entitled "S7 Safety Pharmacology Studies for Human Pharmaceuticals", prepared under the auspices of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use. Written comments were requested by September 6, 2000.

Based on a review of the draft guidance, comments concerning several sections of the document are being submitted. For the sake of clarity, the specific aspects of the sections being addressed have been restated.

Section 2.4.1

"*In the absence of adverse effects on Safety Pharmacology parameters, the highest dose should equal or exceed those doses producing some adverse effects in studies of similar route and duration.*"

In most institutions, Safety Pharmacology studies are typically conducted prior to initiating toxicology investigations. In the absence of adverse effects in Safety Pharmacology studies, the toxicology study is likely to be the study in which dose-limiting toxicity is observed. Therefore there is a conflict in the strategy between having Safety Pharmacology data in advance of toxicology data in order to make appropriate decisions regarding the future development of a new drug and the potential need to produce toxicology data in advance to select doses for Safety

Pharmacology studies. In fact, in some institutions, data from Safety Pharmacology are used to select doses for toxicology studies. It is recommended that the guidance provide sufficient flexibility to allow dosing to a level that is reasonably justified.

Section 2.10.3

"*Safety pharmacology effects on systems listed section 2.8 should be assessed prior to approval unless not warranted, in which case this should be justified*".

The presentation of a justification for not conducting any of an infinite number of studies, as described in section 2.8, should be presented. The assumption is that the following encompassing statement will satisfy the expectations of the guidance, "Studies of other systems are not necessary for this compound since existing data from other preclinical and clinical studies did not raise a cause for concern regarding human safety". However, clarification is needed as to where a statement such as this should be presented.

Schering appreciates the opportunity to provide comments on this draft guidance.

Respectfully submitted,

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